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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/672,843	09/28/2000	Lee G. Dante	OREX.004DD	7299
20995	7590	12/31/2007	EXAMINER	
KNOBBE MARTENS OLSON & BEAR LLP 2040 MAIN STREET FOURTEENTH FLOOR IRVINE, CA 92614			THOMAS, TIMOTHY P	
		ART UNIT	PAPER NUMBER	
		1614		
		NOTIFICATION DATE	DELIVERY MODE	
		12/31/2007	ELECTRONIC	

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>
	09/672,843	DANTE, LEE G.
	<b>Examiner</b>	<b>Art Unit</b>
	Timothy P. Thomas	1614

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 6/31/05.
- 2a) This action is FINAL.                    2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-25 is/are pending in the application.
  - 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 1-25 is/are rejected.
- 7) Claim(s) 1-8, 14 and 21 is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.
 

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a) All    b) Some \* c) None of:
    1. Certified copies of the priority documents have been received.
    2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
    3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Reissue Applications***

1. The objection to the reissue oath/declaration, of the Office Action of 11/08/2002, is withdrawn, due to the filing of the Reissue Application Declaration By the Inventor, filed 12/30/2002.
2. Prosecution as to the merits is reopened.
3. Applicant is advised that the 7½-year maintenance fee for the patent 6,034,091 has not been paid and was due in September, 2007.
4. Claims 10-13, 16-18, and 23-25 are rejected under 35 U.S.C. 251 as being based upon new matter added to the patent for which reissue is sought. The added material which is not supported by the prior patent is as follows:

The prior patent does not disclose any concentrations for the antidepressant fluoxetine. Therefore the concentration ranges of fluoxetine are new matter.

### ***Claim Objections***

5. Claims 8, 14, and 21 are objected to because of the following informalities: the specie "nalmefene" is recited twice on the 2<sup>nd</sup> and 3<sup>rd</sup> lines of the claims. Appropriate correction is required.
6. Claims 1-7 are objected to because of the following informalities: the terms "pharmacologically", in the 5<sup>th</sup> line of claim 1, and "lithium", in the 8<sup>th</sup> line of claim 1, are misspelled; the use of "pharmacologically salts and ester" in the 4<sup>th</sup> line of claim 6 is grammatically incorrect. Appropriate correction is required.

***Claim Rejections - 35 USC § 112***

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1, and 3-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase, "an opioid antagonist having a pentacyclic nucleus structurally analogous to naltrexone, naloxone, and nalmefene" does not make clear what structural feature is required for the opioid antagonist, other than the pentacyclic core of the three named compounds. It is not clear what moieties would fall within the metes and bounds of "structurally analogous to" the pentacyclic nucleus of the claimed compounds.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 10-13, 16-18, and 23-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant has not disclosed any concentrations for fluoxetine in the specification. Therefore the concentration ranges do not have written support in the specification, and are new matter.

11. Claims 1-12, 14-17, 19-24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is not in possession of the genus "an opioid antagonist having a pentacyclic nucleus structurally analogous to naltrexone, naloxone, and nalmefene" (claim 1) or the genus "pharmacologically effective esters" of any of the active drugs.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); *In re Gostelli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966." *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

"A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by

structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163. The MPEP does state that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP § 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation

between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient.” MPEP § 2163. While all of the factors have been considered, a sufficient amount for a *prima facie* case are discussed below.

In the instant case, the claims are drawn to a method of treating depression associated with alcoholism, or a method of treating alcoholism and depression associated therewith comprising the administration of an opioid antagonist, such as naltrexone, and an antidepressant, such as fluoxetine, or a pharmaceutical composition or a pharmaceutical kit containing the same two active compounds.

*(1) Level of skill and knowledge in the art:*

The level of skill and knowledge in the art is high.

*(2) Partial structure:*

Opioid antagonists disclosed include nalmefene, naltrexone, naloxone; besides the core structure of these compounds (pentacyclic nucleus), no “structurally analogous moiety is disclosed.

No examples or partial structures of any ester of an opioid antagonist or of any ester of an antidepressant have been given, except for the “ester” functional group.

*(3) Physical and/or chemical properties and (4) Functional characteristics:*

The opioid antagonist will have the property of antagonist of an opioid receptor.

*(5) Method of making the claimed invention:*

No method of making any compound or synthesizing any ester of a drug is disclosed.

As stated *supra*, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable that claim(s) 1-12, 14-17, 19-24 is/are broad and generic, with respect to all possible compounds encompassed by the claims. The possible structural variations are limitless to any opioid antagonist having a pentacyclic nucleus structurally analogous to naltrexone, naloxone, and nalmefene or any ester of an opioid antagonist or any ester of an antidepressant. Although the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the compounds beyond those compounds specifically disclosed in the examples in the specification. Moreover, the specification lacks sufficient variety of species to reflect this variance in the genus. While having written description of the compound species recited in the claims and compounds identified in the specification tables and/or examples, the specification does not provide sufficient descriptive support for the myriad of compounds embraced by the claims.

The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention.

See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

### ***Claim Rejections - 35 USC § 103***

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

13. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

14. Claims 14 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kitchell, et al. (WO 92/19226 A1; 1992 Nov 12).

Kitchell teaches controlled, sustained release delivery systems (pharmaceutical compositions) useful for treating an individual for drug dependence, such as alcohol (p. 5, 2<sup>nd</sup> paragraph); drug substitutes for alcohol include naltrexone and fluoxetine (p. 6, "Alcohol"; claim 36); a method of treating an individual for drug dependence comprising administering a system to the individual that releases an amount of drug substitute effective to diminish the individual's desire for a drug of abuse for at least one day (claim 1); kits useful in treating drug dependence (claims 37, 43). Kitchell does not teach a combination of naltrexone and fluoxetine in the same composition, a method of treating alcohol dependence or a pharmaceutical kit. It would have been obvious to one skilled in the art at the time of the invention to combine both naltrexone and fluoxetine in the same composition, method of treating alcoholism and pharmaceutical kit, with an expectation of success, since both drugs are taught as useful for treating alcohol dependence. The motivation to combine the two drugs is that both drugs are recognized as equivalent for the same purpose (treating alcohol dependence).

15. Claims 1-13, 15-18, and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kitchell, et al. (WO 92/19226 A1; 1992 Nov 12) as applied to claims 14 and 21 above, and further in view of Barnhart (publisher; "Physicians' Desk Reference; 1991 45<sup>th</sup> Ed.; Dista, "Prozac", pp. 902-904; DuPont, "Trexan", pp. 932-934).

Kitchell teaches the optimum dose range, where the drug exhibits maximum therapeutic effect and minimum adverse side effects is determined empirically, for any drug substitute. Kitchell does not teach doses for fluoxetine or naltrexone or a method of treating depression or a method of treating alcoholism and depression associated

with alcoholism in the same patient. Barnhart teaches fluoxetine hydrochloride is indicated for the treatment of depression (p. 902, "Indications and Usage") and doses equivalent to 20 mg fluoxetine may be sufficient to obtain a satisfactory antidepressant response, controlled trials used to support the efficacy of fluoxetine used doses ranging from 20 mg-80 mg/day, dosed each morning (p. 904, "Dosage and Administration", 1<sup>st</sup> paragraph); naltrexone hydrochloride is available in 50 mg scored tablets (p. 932, "Description"); initial dosing of 25 mg is followed by the rest of the dose after a waiting period (p. 934 "Dosage and Administration, #3), maintenance treatment dosing for blockade of the pharmacologic effects of exogenously administered opioids is 50 mg every 24 hours, 100 mg every other day or 150 mg every third day (p. 932, "Indications and Usage"; p. 934, middle, "Maintenance Treatment"). It would have been obvious to one of ordinary skill in the art at the time of the invention to utilize the doses taught by Barnhart in the compositions and kits of Kitchell for the treatment of alcoholism, and to optimize the doses as suggested by Kitchell, with the potential of administering even lower doses of each drug in combination than dosages taught for each single drug administration. Such routine optimization would have yielded doses within the ranges of the instant claims. The motivation to optimize doses would have been to find the optimal conditions for treating alcoholism. It would also have been obvious to use the combination in the treatment of patients with both alcoholism and depression, since fluoxetine has both properties. It would also have been obvious to administer the combination to a depressed patient that is concomitantly being treated for an anxiety disorder with a benzodiazepine, mania being treated with lithium or a convulsive

disorder being treated with an anticonvulsive compound, although care should be taken with such patients, since these conditions have been observed as side effects of fluoxetine (p. 902, "Precautions"). It would have been obvious at the time of the invention to treat such conditions with the appropriate drugs for those conditions along with the combination therapy. The motivation for concomitant treatment of more than one condition is to address the multiple clinical conditions presenting in the patient.

***Interference***

16. The request for interference filed 9/9/2002 is acknowledged. However, examination of this application has not been completed as required by 37 CFR 41.102(a). Consideration of a potential interference is premature. See MPEP § 2303.

***Conclusion***

17. No claim is allowed.  
18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Timothy P. Thomas whose telephone number is (571) 272-8994. The examiner can normally be reached on Monday-Thursday 6:30 a.m. - 5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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